

1/24/2000. Applicant is aware of the defective declaration and will forward a new corrected declaration when it becomes available.

Rejection under 35 U.S.C. §103(a)

Claims 1-22 stand rejected under 35 U.S.C. 103(a) as being unpatentable over the WO 97/12630 in view of Ragab U.S. 6,346,524 and Kline U.S. 6,180,096 or WO 95/13090.

Per Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966) and MPEP § 2144, the criteria for a prima facie case of obviousness are:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence in the application indicating obviousness or nonobviousness.

When making a rejection under 35 U.S.C. § 103, the Examiner has the burden of establishing a prima facie case of obviousness. In re Fritch, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992). The Examiner can satisfy this burden only by showing an objective teaching in the prior art, or knowledge generally available to one of ordinary skill in the art, which would lead an individual to combine the relevant teachings of the references [and/or the knowledge] in the manner suggested by the Examiner. Id.; In re Fine, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988).

The mere fact that the prior art could be modified does not make the modification obvious unless the prior art suggests the desirability of the modification. In re Fritch, 23 U.S.P.Q.2d at 1784; In re Laskowski, 10 U.S.P.Q.2d 1397, 1398 (Fed. Cir. 1989); In re Gordon, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984).

"It is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious....'[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.'" In re Fritch, 23 U.S.P.Q.2d at 1784 (quoting In re Fine, 5 U.S.P.Q.2d at 1600).

Applicant respectfully traverses the rejection and presents the following comments. Because of the differences between the scope of the prior art and the claimed invention, per the first and second Graham factors, applicant respectfully suggests that a prima facie case of obviousness cannot be established.

Applicant claims a method of treatment using therapeutically effective amounts of temozolomide in combination with **pegylated** interferon alpha. Therapeutically effective amounts temozolomide and pegylated interferon alpha are described on page 3, lines 16-27 and pages 6-7, lines 25, et al. **Pegylated** interferon alpha is described on page 4, lines 12-20 of the specification, as the polyethylene glycol modified conjugates of interferon alpha.


WO 97/12630 discloses the combination therapy of temozolomide and, interferon alpha, specifically interferon alpha 2b (see generally, Abstract, pages 4-5 of the specification and claims 1-21). However, as acknowledged by the Examiner, WO 97/12630, does not disclose the use of PEG₁₂₀₀₀-interferon alpha 2b, the specific concentrations of PEG₁₂₀₀₀-interferon alpha 2b and the formation of a kit. The Examiner references Kline and WO 95/13090 for their disclosure of PEG interferon alpha 2b (see generally, Abstract, for both references). However, there is no teaching or suggestion in Kline, WO 97/12630 or WO 95/13090 to combine **pegylated** interferon alpha 2b in combination with temozolomide to treat cancer. In fact, WO 97/12630 teaches away from the applicant's invention by the fact that it uses **non-pegylated** alpha interferon rather than **pegylated** interferon alpha 2b. **Pegylated** interferon alpha and **non-pegylated** interferon alpha, as used in WO 97/12630 are distinct from one another. (See applicant's specification, page 4, lines 12-23 and page 5, lines 1-27). Thus, WO 97/12630 cannot be relied upon to render the inventor's application obvious. Further, Ragab merely discloses the use of temozolomide **alone**, (see generally, Abstract, col. 2, lines 31-45 and claims 1-11 of Ragab) there is no teaching or suggestion of combination therapy with interferon alpha, let alone combination therapy with **pegylated** interferon alpha-2b. In addition, applicant believes that one of ordinary skill in the art would not necessarily consider Ragab's mono therapy of temozolomide to treat cancer when practicing the combination temozolomide and **pegylated** interferon alpha-2b therapy described by

the applicant's invention, due to the additional presence of **pegylated** interferon alpha-2b in the applicant's pending invention. Finally, neither Ragab, Kline, WO 97/12630 or WO 95/13090 contain any teaching or suggestion to combine any of them in order to teach the applicant's claimed invention, temozolomide in combination with **pegylated** interferon alpha 2b. Applicant respectfully suggests that per the first and second Graham factors, these differences in the scope and contents of the claimed invention from the cited art preclude a finding of obviousness. Therefore, applicant respectfully submits that the claimed invention is not obvious in light of Ragab, Kline, WO 97/12630 and WO 95/13090. Reconsideration and withdrawal of this ground of rejection is respectfully urged.

In view of the foregoing, applicant submits that the application, as pending, is in condition for allowance and courteously solicit a Notice of Allowance.

The Examiner is requested to call the undersigned attorney on any matter connected with this application.

Respectfully submitted,



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